



King's Research Portal

Document Version

Early version, also known as pre-print

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Puri, T., Chalkidou, A., Roy, A., Henley-Smith, R., Barber, P. R., Guerrero-Urbano, T., Oakley, R., Simo, R., Jeannon, J-P., McGurk, M., Odell, E., O'Doherty, M., & Marsden, P. (2013). A Method for Accurate Spatial Registration of PET Images and Histopathology Slices. In *National Cancer Research Institute (NCRI) Cancer Conference* (N/A ed., Vol. N/A, pp. N/A). <http://conference.ncri.org.uk/abstracts/2013/abstracts/LB66.htm>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

A METHOD FOR ACCURATE SPATIAL REGISTRATION OF PET IMAGES AND HISTOPATHOLOGY SLICES

Tanuj Puri^{1,*}, Anastasia Chalkidou¹, Arunabha Roy¹, Rhonda Henley-Smith², Paul R. Barber^{3,4}, Teresa Guerrero-Urbano⁵, Richard Oakley⁵, Ricard Simo⁶, Jean-Pierre Jeannon⁶, Mark McGurk⁶, Edward Odell², Michael O'Doherty¹, Paul Marsden¹

¹Kings College London, Imaging Sciences and Biomedical Engineering, London, UK; ²Kings College London, Pathology Department, London, UK; ³University of Oxford, Department of Oncology, Oxford, UK; ⁴Kings College London, Institute for Mathematical and Molecular Biomedicine, London, UK; ⁵Department of Clinical Oncology, Guy's & St Thomas' NHS Foundation Trust, London, UK; ⁶Department of Head & Neck Surgery, Guy's & St. Thomas' Hospital NHS Trust, London, UK

INTRODUCTION

- An accurate alignment of **histopathology** sections and **PET images** is important for **radiopharmaceutical validation studies**¹.
- We developed a method to align PET and **histology** images obtained in a **routine pathology laboratory setting** and assessed its accuracy.
- The method can be applied to **non-parallel, non-contiguously cut** and **non-mega-block sized** histology slices.

METHODS

- Subjects with **head and neck cancer** underwent a **⁶⁴Cu-ATSM PET-CT** scan a week before surgery.
- After surgery, **sea urchin spines** (**Figure 1a**), which can be **identified with CT, optically** and **histologically**, were inserted into the specimen to act as **fiducial markers**.
- The specimen was **fixed** and **scanned CT ex-vivo**. After slicing, blockface images were obtained for visual reference.
- From these thick sectioned slices, a subsection of tissue that included tumour and markers was extracted and embedded in paraffin blocks of size **30x21 millimetre (mm)**.
- Subsequently **microtome sectioning** and **haematoxylin and eosin** staining was performed to acquire thin slides and digitised using a microscope.
- The methodology used to align PET and histology is described in **Figure 1b**.

RESULTS

- The PET and histology registered to CT ex-vivo are shown in **Figure 2**.
- The accuracy for registration of **in-vivo to ex-vivo CTs** was **2.90±0.06mm**, and for registration of **histology to ex-vivo CT** was **1.69±0.70mm**.
- The **total registration error** between **PET-Histology** for **10 histology samples** was **6.39±0.21mm** (**Table 1**).
- The **largest error in the PET-Histology registration process** is due to the **systematic PET-CT registration error**.

FIGURE 1 (a: Left): A 5-micrometre (µm) thin tissue section with **sea urchin spine** cut orthogonally and scanned under a light microscope. **(b: Right):** The first step of the methodology is to align PET and CT (in-vivo) images with an accuracy² of **5.4mm** using **mutual information based rigid registration**. In the second step, the original high resolution CT ex-vivo specimen is resampled to match CT in-vivo voxel size such that **anatomical landmarks were** used for in-vivo and ex-vivo CT registration. Finally, the original high resolution CT ex-vivo is orientation corrected to match the down-sampled CT ex-vivo such that the **Inter-marker distances** between fiducial markers were used for histology to ex-vivo CT registration. Errors were assessed using a leave-one-out strategy³.

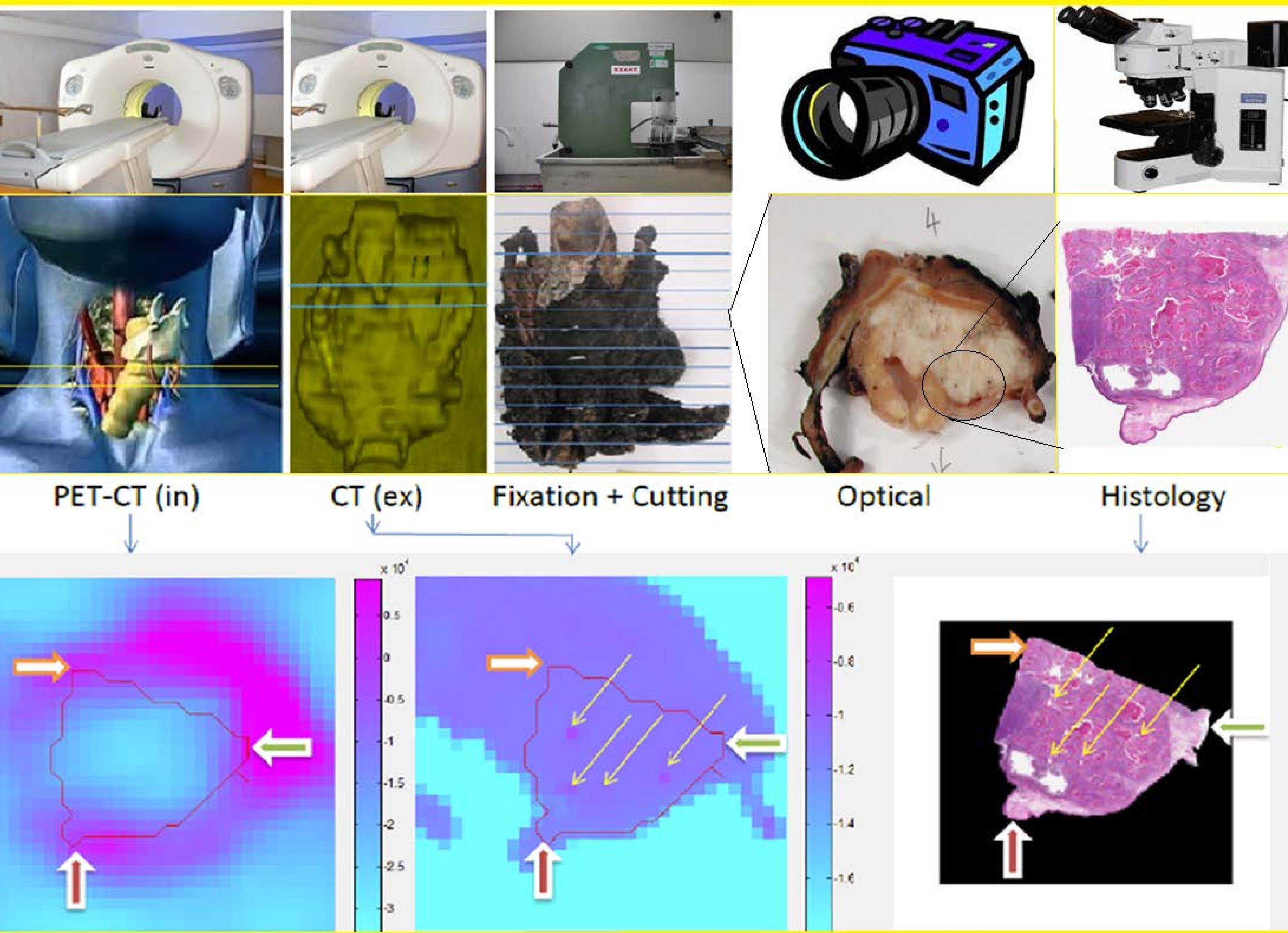


FIGURE 2: The top row shows (from left to right) a PET scanner, CT scanner, band-saw used to slice larynx, optical camera and a light microscope. The middle row shows images of PET-CT in-vivo, CT ex-vivo, images of ex-vivo specimen fixed and sliced images taken with a camera and histology sample digitised using a light microscope. The bottom row shows registered images of PET, CT ex-vivo and histology. **Regions in PET and CT ex-vivo that correspond to histology are marked with red outline**. Yellow markers show the sea urchin spine markers on CT ex-vivo and histology images.

	REFERENCE	TRE-Mean(L-1-O)	TRE-Max(L-1-O)	TRE(mean)
Samples	PETin-CTin	CTin-CTex	CTex-Histology	TOTAL
1	5.40	2.83	0.91	6.16
2	5.40	2.83	1.47	6.27
3	5.40	2.83	2.58	6.62
4	5.40	2.83	1.23	6.22
5	5.40	2.94	0.93	6.22
6	5.40	2.94	2.00	6.47
7	5.40	2.94	2.96	6.82
8	5.40	2.94	1.81	6.41
9	5.40	2.94	1.04	6.24
10	5.40	2.94	1.94	6.45
MEAN	5.40	2.90	1.69	6.39
SD	0.00	0.06	0.70	0.21

TABLE 1: The table shows (from left to right) the **registration errors in millimetres** for **ten histology samples**. TRE corresponds to target registration error. L-1-O correspond to leave-one-out. PETin corresponds to positron emission tomographic image obtained in-vivo. CTin corresponds to computed tomography image obtained in-vivo. CTex corresponds to computed tomography image obtained ex-vivo.

CONCLUSION

We have developed a semi-automated registration method to align PET and histology images (**Figure 2**) with a registration accuracy of **6.39mm** (**Table 1**) which is comparable to the PET spatial resolution.

*CORRESPONDING AUTHOR

tanujpuri82@gmail.com
tanuj.puri@kcl.ac.uk

REFERENCES

- [1] Gerlinger M. et al., New Engl J Med. 366:883–892, 2012
- [2] Rizzo G. et al., Q J Nucl Med Mol Imaging, 49(3):267-79, 2005
- [3] Caldas-Magalhaes J. et al., Int. J. Radiation Oncology Biol Phys, 82:289-298, 2012

ACKNOWLEDGEMENTS

We would like to acknowledge King's College London and UCL Comprehensive Cancer Imaging Centre. Funded by the CRUK and EPSRC in association with the MRC and DoH (England). The authors would like to thank the staff at the head and neck bio bank, the Pathology laboratory at Guys' Hospital and PET Imaging Centre at St. Thomas' Hospital for their excellent technical support. This research is supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London. The views expressed here are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.



Engineering and Physical Sciences Research Council